REMARKS

Claims 1, 6, 9, 14-22 and 27-30 are pending, with Claims 3-5, 7-8, 10-13 and 23-26 cancelled, and with Claims 21-22 withdrawn as being directed to a nonelected invention. A listing of the claims with appropriate status identifier begins on page 2.

By the present amendment, Claims 23-26 are formally canceled in view of the indication "not entered" for Claims 23-26 contained in the Advisory Action mailed July 6, 2007.

By the present amendment, Claims 1 and 14 are amended to define the invention with greater particularity. Applicants respectfully submit that amendment to Claims 1 and 14 place the claims in condition for allowance, or at a minimum in better condition for appeal, and that the subject matter of Claims 1 and 14 as amended must, of necessity, have already been considered by the Examiner, obviating any additional search burden. Accordingly, Applicants respectfully request entry of the present amendment in accordance with MPEP § 714.13.

Support for the amendment to Claims 1 and 14 may be found in the specification at, e.g., paragraph [0002], [0018], [0025] and [0071]. Reference to paragraph numbers of the specification herein refer to U.S. Patent Application Publication No. US2005/0070472. The amendment introduces no new subject matter.

With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover, have not acquiesced to any rejections or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Applicants respectfully request rejoinder of Claims 21 and/or 22 in the event that Claims 1 and/or 14 are allowed, from which Claims 21-22 depend, respectively. Applicants have carefully considered the points raised in the Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance subject to the requested rejoinder of Claims 21-22.

Rejections under 35 U.S.C. §103

The rejection of Claims 1, 6, 9, 14-20 and 27-30 under 35 U.S.C. §103(a) as allegedly being unpatentable over Young *et al.* (U.S. Pat. No. 5,677,279; hereinafter "Young") in further view of Brain *et al.* (U.S. Pat. No. 7,045,533; hereinafter "Brain") and Jorgensen *et al.* (U.S. Pat. No. 4,370,317; hereinafter "Jorgensen"), is respectfully traversed.

Claim 1 as amended is directed to a method of treating acute pancreatitis in a mammalian subject by administration of an effective amount of an amylin or an amylin analog, wherein the amylin analog has amylin agonist activity, and wherein the treatment comprises reducing or inhibiting the level of inflammation, enzymatic activity or enzymatic secretion in pancreatic cells. Claim 14 as amended is directed to improving a method of treatment for acute pancreatitis of a mammalian subject by administration of an amylin or an amylin analog in addition to an agent or regimen used to treat acute pancreatitis, wherein the amylin analog has amylin agonist activity and wherein the treatment comprises reducing or inhibiting the level of inflammation, enzymatic activity or enzymatic secretion in pancreatic cells.

The claimed invention relies on Applicants' discovery that administration of a compound with amylin agonist activity can be used to treat acute pancreatitis, an inflammatory process in which pancreatic enzymes are released into the pancreas and surrounding tissues. See e.g., specification paragraph [0072]. A key discovery by Applicants is provided in Example 1, which demonstrates the unpredicted benefit upon progression of acute pancreatitis in an animal model, i.e., reduction of pancreatic enzymes in the <u>blood</u> of the test mammal. As well known in the art, pancreatic enzymes, e.g., amylase and lipase, are not normally found in the blood. Indeed, the specification at paragraph [0009] discloses that "[i]n contrast to acute or reoccurring acute pancreatitis, serum amylase and lipase levels are not elevated in patients with chronic pancreatitis." Rather, pancreatic toxins and enzymes (e.g., amylase and lipase) in the blood as a consequence of tissue damage at the pancreas, e.g., acute pancreatitis. See e.g., specification paragraph [0072]. Thus, the reduction of pancreatic enzymes in the blood in Example 1 is indicative of disease amelioration. Furthermore, the aforementioned treatment of acute pancreatitis is separate from relief of pain due to pancreatitis. See e.g., specification paragraph

[0073]. Additionally, the reduction in pancreatic enzymes in the blood is distinct and dissociable from the reduction in enzyme in exocrine secretions described in Example 2. Indeed, Example 2 describes a physiologic non-disease related effect of amylin upon digestive secretions that is independent of changes in enzyme activity in the blood (i.e., Example 1). Furthermore, blockade of enzymatic secretion, as e.g., with anti-cholinergic drugs has not been shown useful. See e.g., specification paragraph [0013]. Accordingly, enzyme inhibition *per se* does not predict the disease amelioration demonstrated in Example 1 and claimed in Claims 1 and 14.

In contrast, Young merely describes the use of an amylin or amylin agonist for treating or preventing pain. Thus, Applicants disagree with the Examiner's assertion (Office Action, page 2, lines 22-23) that "Young teaches a method of relieving the pain and/or treating painful inflammation disorders ... (emphasis added)." The Examiner has provided no evidence that Young contemplates treatment of acute pancreatitis. Indeed, Young contemplates treatment of pain, not treatment of acute pancreatitis. Accordingly, Young does not teach or suggest the use of an amylin or an amylin analog having amylin agonist activity for treating acute pancreatitis as required by the current claims.

In order to cure the deficiency of Young, the Examiner asserts (Office Action, page 3, lines 5-6) that "Brain et al. beneficially teach that pancreatitis is a very painful inflammation condition and/or inflammation disorder ... ." Applicants respectfully submit that the Examiner has provided no evidence that Brain contemplates treatment of acute pancreatitis with an amylin or an amylin analog having amylin agonist activity. The Examiner further asserts (Office Action, page 3, lines 7-9) that "Jorgensen et al. beneficially teach that pancreatin treats pancreatitis ..." Applicants respectfully submit that the Examiner has provided no evidence that Jorgensen contemplates treatment of acute pancreatitis with an amylin or an amylin analog having amylin agonist activity.

In view of Young and Brain, the Examiner further alleges (Office Action, page 3, lines 10-19) that

> [i]t would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have administered the same amylin analog as the

> claimed invention's amylin analog of 25,28,29 Pro-h-amylin and an analgesic to treat the painful inflammation disorder of pancreatitis in a mammalian subject because Young teaches that the amylin analog of 25,28,29 pro-h-amylin and an analgesic treats painful inflammation treats painful inflammation disorders and Brain teaches that pancreatitis is a painful inflammation disorder. Thus, when the same amylin analog as the claimed invention's analog of 25,28,29 pro-h-amylin in combination with an analgesic are administered to a mammalian subject for treating painful inflammation disorders, it would intrinsically treat the painful inflammation disorder of pancreatitis (*emphasis added*).

Applicants respectfully submit that the Examiner's incorporation (Office Action, page 2, line 21) of an "analgesic" claim element (see emphases *supra*) administered with the amylin or amylin analog is in error because the Examiner has apparently misapprehended the invention. Indeed, use of an analgesic (as required in the rejection) does not form a claim element of either of Claims 1 or 14. Accordingly, Applicants respectfully submit that the current rejection is irrelevant with respect to Claims 1, 6, 9, 14-17, 19-20, and 27-30, which claims do not require an analgesic element, and Applicants respectfully request allowance of at least Claims 1, 6, 9, 14-17, 19-20, and 27-30.

In further view of Young and Jorgensen, the Examiner alleges (Office Action, page 3, line 19 to page 4, line 3) that

> ... it would have been obvious to modify Young's administration's method of administering the same amylin analog as the claimed inventions amylin analog of 25,28,29Pro-h-amylin in combination with an analgesic to include the teaching of Jorgensen which states a pancreatic enzyme such as pancreatin is well known in the art for treating pancreatitis because the above combined teachings would create an improve method of administering of treating the painful inflammation disorder of pancreatitis in a mammalian subject (*emphasis added*).

Applicants respectfully submit that the Examiner's incorporation (Office Action, page 2, line 21) of a "pancreatic enzyme" claim element (see emphasis *supra*) administered with the amylin or amylin analog is in error because the Examiner has apparently misapprehended the invention. Indeed, use of a pancreatic enzyme (as required in the rejection) does not form a claim element of either of Claims 1 or 14. Accordingly, Applicants respectfully submit that the current rejection is irrelevant with respect to Claims 1, 6, 9, 14-17, 18, 20, and 27-30, which claims do

not require a pancreatic enzyme element, and Applicants respectfully request allowance of at least Claims 1, 6, 9, 14-17, 18, 20, and 27-30.

Regarding the current obviousness rejection, the Supreme Court has addressed the issue of obviousness in *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727 (2007). The Court stated that the Graham factors (*Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966)), still control an obviousness inquiry. Those factors are: 1) "the scope and content of the prior art"; 2) the "differences between the prior art and the claims"; 3) "the level of ordinary skill in the pertinent art"; and 4) objective evidence of nonobviousness. *KSR*, *id.* at 1734 (quoting *Graham*, *id.* at 17-18). While the *KSR* Court rejected a rigid application of the teaching, suggestion, or motivation ("TSM") test in an obviousness inquiry, the Court acknowledged the importance of identifying "a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does" in an obviousness determination. *KSR*, *id.* at 1731. In this regard, "[r]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR*, *id.* at 1741 (quoting *In re Kahn* 441 F.3d 977, 988 (Fed. Cir. 2006) (*emphasis added*). Further, the Court recognized that the prior art must suggest a predictable outcome to establish a *prima facie* case of obviousness (*emphasis added*). See, e.g., *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.* 492 F.3d 1350, 83 U.S.P.Q.2d 1169 (Fed. Cir. 2007).

Regarding the currently asserted combination of references, there is no reasonable expectation of success in combining the references so as to arrive at the presently claimed methods. Therefore, the references do not provide a predictable outcome for treating acute pancreatitis, as required by the law. See *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd., (id.)* Specifically, although Brain may allegedly allude to pancreatitis as a painful condition, and Young and Brain may allegedly disclose general analgesic properties, there is no rational underpinning for the proposition that analgesic compounds can actually treat acute pancreatitis. See *KSR*, (*id.* at 1741). In particular, the Examiner has provided no objective reasoning with rational underpinning why the treatment of pain, as disclosed e.g. by Young and/or Brain, would

be expected to treat acute pancreatitis as claimed. Furthermore, the Examiner has provided no objective reasoning with rational underpinning as to why one skilled in the art when confronted with the universe of all possible analgesic compounds would be directed to specifically select an amylin or an amylin analog having amylin agonist activity.

Apparently, in construing the claims, the Examiner has improperly equated treating pancreatitis with providing analgesia, which construction is expressly deprecated in the specification. See e.g., specification paragraph [0002]. Furthermore, this construction of the claims by the Examiner is contrary to the doctrine of claim interpretation. The doctrine of claim differentiation is "based on the common sense notion that different words or phrases used in separate claims are presumed to indicate that the claims have different meanings and scope." *Karlin Tech. Inc. v. Surgical Dynamics, Inc,* 177 F.2d 968, 971-72 (Fed. Cir. 1999). Claim 3 as originally filed requires that the method "simultaneously treats pancreatitis and the pain associated therewith." See also specification paragraph [0073]. If, as under the Examiner's apparent claim construction, providing analgesia is synonymous with treating pancreatitis, then Claim 3 would have been redundant. In accordance with the doctrine of claim differentiation, the separation of treating pancreatitis and alleviating pain associated with pancreatitis in both the claims and the specification requires a claim construction different from that used by the Examiner to support the present rejection.

Indeed, none of the cited references, either alone or combined, teach that an amylin or an amylin analog having amylin agonist activity can treat acute pancreatitis as claimed. Rather, it was Applicants' discovery that an amylin or an amylin analog having amylin agonist activity could be used to treat acute pancreatitis, by e.g., reducing or inhibiting the level of inflammation, enzymatic activity or enzymatic secretion in pancreatic cells. See e.g., specification at paragraph [0025]. Accordingly, alone or combined, the cited references do not teach or suggest with any rational underpinning or predictable outcome that an amylin or an amylin analog having amylin agonist activity can be used to treat acute pancreatitis. Thus, the cited references cannot support a *prima facie* case of obviousness. Accordingly, Applicants respectfully request reconsideration and withdrawal of the current rejection and allowance of the current claims.

CONCLUSION

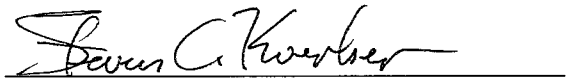
Applicants believe that all issues raised in the Office Action have been properly addressed in this response. Accordingly, reconsideration and allowance of the pending claims is respectfully requested. If the Examiner feels that a telephone interview would serve to facilitate resolution of any outstanding issues, the examiner is encouraged to contact Applicants' representative at the telephone number below.

No additional fees are believed due for this submission. However, if a fee is due, the Commissioner is hereby authorized to charge payment of any fees associated with this communication, to Applicant's Deposit Account No. 010535 referencing Docket No. 0101-UTL-0. Additionally, the Commissioner is hereby authorized to charge payment or credit overpayment of any fees during the pendency of this application to Applicant's Deposit Account No. 010535.

Date: October 20, 2008

Respectfully submitted,

AMYLIN PHARMACEUTICALS, INC.



Steven C. Koerber
Reg. No. 54,233

Amylin Pharmaceuticals, Inc.
9360 Towne Centre Drive
San Diego, California 92121
Phone (858) 754-4121
Facsimile (858) 552-1936